REMARKS

Favorable reconsideration and allowance of the present application are respectfully requested in view of the following remarks.

Claims 1-6, 9-13, and 39-45 are pending in the present application including independent claim 1. In the Office Action, independent claim 1 was rejected under *35 U.S.C. § 103(a)* as being obvious over WO 97/09620 to Rylatt, et al. in view of U.S. Patent No. 5,670,381 to Jou, et al. Rylatt, et al. is directed to a method that involves the use of a test zone containing an analyte receptor capable of binding to the target analyte and a calibration zone containing a calibration agent receptor capable of binding a calibration agent. The signals associated with the labels at the test zone and calibration zone are measured to determine the target analyte in the test sample. In Fig. 2, for instance, a device is shown for detecting D-dimer. The device includes a test zone 204 containing an analyte receptor 215 (i.e., monoclonal antibody DD-1D2/48 1D2 antibody) that binds to D-dimer when complexed to an analyte detection agent 208 (i.e., D-dimer binding monoclonal antibody DD-3B6/22 labeled with colloidal gold). The device also includes two calibration zones 210, 211 containing BSA labeled with biotin 214, 216 for binding to the calibration agent 209 (i.e., streptavidin labeled with colloidal gold). Further, the device includes a procedural control zone 212 containing an anti-mouse antibody 217 capable of specifically binding the analyte detection agent 208.

The Office Action asserts that the procedural control zone 212 of Rylatt, et al. is akin to the claimed compensation zone. Applicants respectfully disagree. As is well known to those skilled in the art, a procedural control zone is employed simply to indicate to a user that the assay is working properly. In stark contrast, the claimed

compensation zone is an integral part of the assay and is used in the determination of the analyte concentration. That is, as explained in the present application, the signal from the compensation zone can compensate for the lost signal resulting from those probes that are embedded too deep within the interior of the assay device and/or those probes that exhibit self-quenching. In this regard, independent claim 1 requires that the *amount of the analyte within the test sample is proportional to the ratio of the detection signal intensity to the compensation signal intensity*, as calibrated by the calibration signal intensity. This limitation simply cannot be satisfied by a "procedural control zone."

Of course, Rylatt, et al. also fails to disclose various aspects of independent claim 1. For instance, as correctly noted by the Examiner, Rylatt, et al. fails to disclose the use of a polyelectrolyte having a net charge opposite to that of the conjugated detection probes. Nevertheless, the Office Action combined Rylatt, et al. with Jou, et al. in an attempt to render obvious independent claim 1. Jou, et al. describes a porous material containing (a) a first reagent zone containing a diffusive indicator (first binding member and label); (b) second reagent containing a diffusive capture reagent (second binding member and first charged substance); and (c) reaction zone containing an immobilized charged substance that has an opposite charge to the first charged substance. In Example 1, for instance, the assay employs an alkaline phosphate-labeled anti-CEA antibody (indicator reagent); an anti-CEA/polyglutanic acid conjugate (capture reagent); and a solid phase coated with Celquat® L-200. With the addition of CEA, complexes form between the indicator reagent, CEA, and capture reagent.

As an initial matter, the systems of Rylatt, et al. and Jou, et al. are so vastly different from each other that one of ordinary skill in the art would not have possibly found it obvious to make the combination proposed in the Office Action. Even if Jou, et al. is combined with Rylatt, et al., however, the resulting combination still fails to disclose each limitation of the present claims. For example, as with most conventional immunoassays, detection is accomplished in Jou, et al. through complexes formed between the analyte (CEA), the binding member of the indicator reagent (anti-CEA), and the binding member of the capture reagent (anti-CEA). The charged substances are used only to enhance the immobilized of these complexes on the solid phase (e.g., porous material), but not as the primary binding mechanism for detection of the analyte. Thus, conjugation of the charged substance of Jou, et al. to the ligand in the control zone of Rylatt, et al. would not lead to the generation of the "compensation signal" as claimed.[1] That is, the signal generated at the control line in Rylatt, et al. would still stem primarily from the specific binding between the biological control ligand and the biological reagent (antibody) conjugated to the nanocrystals.

Thus, for at least the reasons indicated above, Applicants respectfully submit that the present claims patentably define over the cited references, taken singularly or in any proper combination. Applicants emphasize that an invention is not obvious simply because various parts of the claims may be found somewhere in the prior art. If this were the case, virtually every invention would be considered obvious. Instead, the proper standard under *§ 103* is whether the claimed invention *as a whole* when viewing

[1] To even better clarify this distinction, Applicants previously added dependent claim 43, which further requires that the compensation zone is generally free of biological capture reagents.

the teachings of the references *in their entirety*. In this case, as explained above, the present claims are so substantially different from the references, when properly viewed in their entirety, that one of ordinary skill in the art would not have conceivably modified and/or combined the references as suggested in the Office Action.

It is believed that the present application is in complete condition for allowance and favorable action, therefore, is respectfully requested. Examiner DiRamio is invited and encouraged to telephone the undersigned, however, should any issues remain after consideration of this Amendment.

Please charge any additional fees required by this Amendment to Deposit Account No. 04-1403.

Respectfully requested,

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10/30/08
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